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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,223	12/06/1999	DAVID WALLACH	WALLACH-24	9660

1444 7590 01/15/2004

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/445,223	WALLACH ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-8,11,14,15,22-24,29,30,40-49 and 51-54* is/are pending in the application.

4a) Of the above claim(s) *14,15,22,29,30,40-43 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8,11,23,24,44-48 and 51-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☒ Interview Summary (PTO-413) Paper No(s). *01/08/03*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application contains claims drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant adds new claim 54. In a telephonic conversation with Roger Browdy on 01/08/03, Applicant intends for claim 54 to recite an isolated DNA sequence in accordance with claim 44, and not claim 49. Thus claim 54 is related to claim 44 and is not new matter.

Accordingly, claims 5-8, 11, 23-24, 44-48, 51-54 are being examined.

The following are the remaining rejections.

RESTRICTION

Applicant asserts that the present claims are now amended and use the same format of Example 17, and thus the Examiner now should examine both the DNA and protein claims.

Applicant's arguments in paper of 10/16/03 have been considered but are found not to be persuasive for the following reasons:

The restriction requirement has not and will not change in view of the claim amendment, and protein claims are not rejoined with DNA claims, because the

restriction requirement is based on the claims as **originally presented at the time of the restriction requirement.**

The requirement is still deemed proper, and was and is made FINAL, for reasons set forth above, and in previous Office action.

OBJECTION

1. Claim 54 is objected to because claim 54 depends on non-elected, cancelled claim 49.

2. The amendment filed on 10/16/03 is objected to under 35 U.S.C. § 132 because it introduces new matter into the specification. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

Applicant amends the specification on pages 13, 14, and 47 . Applicant asserts that this was an obvious error, which is noted by the Examiner in the corresponding claim language.

It is noted that the correction of the specification in paper of 10/16/03 is not an obvious error. It introduces new matter into the specification.

Applicant is required to cancel the new matter in the response to this Office action.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER

Claims 24, 51-53 remain rejected under 35 USC 112, first paragraph, pertaining to containing subject matter which was not described in the specification, for reasons already of record in paper No:17.

Applicant amends the specification on pages 13, 14, and 47. Applicant argues that the claims are now supported by the specification.

Applicant's arguments in paper of 10/16/03 have been considered but are found not to be persuasive for the following reasons:

Rejection remains. The language "an oligonucleotide molecule consisting of" an antisense sequence of claims 24, 51-53 still introduces new matter, because said language was not supported in the original specification.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Claims 5-8, 11, 23-24, 44-48, 51-52 remain rejected under 35 USC 112, first paragraph, pertaining to lack of enablement of a DNA sequence encoding a polypeptide analog or fragment of SEQ ID NO:1, which analog or fragment potentiates cell death, for reasons already of record in paper No:17.

New claims 54 is rejected for the same reasons of record.

Applicant argues as follows:

1) With respect to the breadth of the claims, ten changes in the 540 residues amounts to less than 2%.

Applicant asserts that Revised interim Written description Guidelines should be instructive also from the standpoint of enablement to the extent that the Office has

conceded that a single example is representative of the entire genus of variants with 95% identity, and thus the claimed analog does not have a particularly wide breadth.

2) The nature of the invention is such that substantial experimentation is reasonably conducted by one of skill in the art. Applicant must not be limited to exemplified embodiments. As long as it is shown the experimentation to determined what falls within the claims is not undue, the enablement requirement is met.

3) As to the level of one of skill in the art, because of the extremely high level of ordinary skill, even complex experimentation is not necessarily undue.

4) As to the predictability in the art, when changing the sequence by less than 2% , there would be an expectation that the function is maintained.

5) Concerning direction provided by the inventor, it is testable in order to determine which will have the claimed function, using routine techniques such as mutagenesis, and cell death assays, disclosed in the specification. Screening using such a standard test, especially in view of the small number of amino acids that may be changed, does not involve undue experimentation.

Further, substantial guidance is provided as to preferred substitution, which would be expected to retain the activity of the B1 protein.

6) Concerning working examples, examples of cell death assays and the effect of B1 proteins in these assays is provided. Mutants If B1 are also tested in Example 3.

Further, additional working examples are not necessary, because the specification discloses how to determine whether any given compound falls within the scope of the claims.

6) Concerning the quantity of experimentation, although substantial experimentation will be necessary, however, a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance. The procedure for making variants of the B1 protein, which have at least 98% identity with the sequence thereof is conventional in the art, such as mutagenesis and cell death assays

The fact that any single amino acid change might have a profound effect or no effect is not really dispositive.

If there is enablement for the DNA of claim 44, there must be enablement for the polypeptides of claim 40 encoded by same and other claims which depend therefrom.

Applicant's arguments in paper of 10/16/03 have been considered but are found not to be persuasive for the following reasons:

It is noted that the polypeptide of claim 40 has not been and will not be examined in the instant application, and therefore, any argument pertaining to claim 40 is moot.

It is further noted that new claim 54 reads on an isolated DNA sequence of claim 44, wherein the entire DNA sequence is a coding sequence encoding said analog polypeptide.

Contrary to Applicant arguments, the function of the claimed variants is not predictable when changing the sequence encoding SEQ ID NO:1 by 2%, because even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristics of a protein, as taught by Burgess e tal, Lazar et al, Tao et al, and Gillies et al, all of record.

The specification however does not teach how to make the claimed variants such that they function as claimed.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the unpredictability of protein chemistry, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

January 08, 2004